

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for generating antigen-binding fragments of an antibody, comprising:

providing an antibody-producing cell line that is growing in a cell media under conditions to express antibodies;

incubating said cell line under conditions to express antibodies into said cell media;

adjusting pH conditions of the cell media to activate at least one endogenous enzyme in said cell media that cleaves said antibodies; ~~and~~

incubating said ~~cell line~~ cell media containing antibodies under said adjusted pH conditions so that said antibodies are cleaved into antigen-binding antibody fragments; and

substantially purifying said antigen-binding antibody fragments.

2. (Original) The method of Claim 1, wherein said antibodies are cleaved into F(ab')₂ fragments.

3. (Previously Presented) The method of Claim 1, further comprising adjusting temperature conditions of the cell media.

4. (Canceled)

5. (Previously Presented) The method of Claim 1, wherein adjusting pH conditions comprises adjusting a pH of the cell media to about pH 3.5.

6. (Original) The method of Claim 1, further comprising inactivating said at least one endogenous enzyme after incubating said cell line.

7. (Currently Amended) The method of Claim 1, ~~further comprising substantially purifying wherein~~ said antigen-binding antibody fragments are substantially purified by affinity chromatography.

8. (Original) The method of Claim 1, wherein said at least one enzyme comprises a serine protease.

9. (Original) The method of Claim 1, wherein said at least one enzyme comprises a cysteine protease.

10. (Original) The method of Claim 1, wherein said at least one enzyme comprises an aspartyl protease.

11. (Original) The method of Claim 1 wherein the cell line comprises cells selected from the group consisting of: Chinese hamster ovary cells, HeLa cells, baby hamster kidney cells, monkey kidney cells, and human hepatocellular carcinoma cells.

12. (Canceled)

13. (Previously Presented) The method of Claim 1 wherein the cell line is provided in a protein free media.

14. (Previously Presented) The method of Claim 1 wherein the cell line is provided in a media comprising a peptone source.

15. (Previously Presented) The method of Claim 1 wherein the cell line is provided in a CD-CHO media.

16. (Previously Presented) The method of Claim 1 further comprising inactivating said at least one enzyme by adjusting a pH of the cell media.

17. (Original) The method of Claim 16 wherein inactivating said at least one enzyme comprises inactivating a cysteinyl enzyme.

18. (Original) The method of Claim 17 further comprising activating an aspartyl enzyme by adjusting the pH of the cell media after endogenous cysteinyl enzyme activity has been reduced.

19. (Currently Amended) A method for producing antigen-binding F(ab')₂ fragments of an antibody, comprising:

providing a cell media comprising a cell line that is growing under conditions to produce a recombinant antibody;

incubating said cell line under conditions to express the recombinant antibody into said cell media;

inactivating endogenous cysteinyl enzyme activity in said cell media containing the recombinant antibody; and

activating endogenous aspartyl enzyme activity in said cell media containing the recombinant antibody by adjusting pH conditions of the cell media, such that said

activating results in cleavage of said recombinant antibody into antigen-binding F(ab')₂ fragments.

20. (Previously Presented) The method of Claim 19 wherein the cell line is provided in a CD-CHO media.

21. (Previously Presented) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adjusting a pH of the cell media.

22. (Original) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adding a cysteinyl enzyme inhibitor to the cell media.

23. (Previously Presented) The method of Claim 22, wherein said cysteinyl enzyme inhibitor is E64.

24. (Canceled)

25. (Original) The method of Claim 19, further comprising purifying said F(ab')₂ fragments from said cell media.

26 – 29 (Canceled)